REMARKS

This Amendment, filed in reply to the Office Action dated September 15, 2010, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 7-23 and 28-30 are withdrawn from consideration as allegedly being directed to non-elected inventions. Claims 1 and 3-6 are rejected. Claim 4 is canceled herewith without prejudice or disclaimer. Claims 1, 3 and 5-23 and 28-30 are amended herewith. The amendments to Claims 5-23 and 28-30 are solely to improve grammar.

Claim 1 is amended herewith to recite incubating a fertilized avian egg to form an early embryo, and microinjecting a replication-deficient retroviral vector coding for an antibody into the early embryo, wherein the microinjection occurs at least 24 hours after the start of the incubation. Support for this recitation can be found throughout the specification as originally filed, and at, for example, page 10, 2nd paragraph. Claim 1 is further amended to recite that the antibody content is not lower than 5μg/ml in blood, not lower than 1μg/ml in egg white, and not lower than 1μg/ml in egg yolk. Support for this recitation can be found throughout the specification as originally filed, and at, for example, page 8, 3rd paragraph.

Claim 3 is amended to improve clarity and conciseness. Support for the amendments to Claim 3 can be found throughout the specification as originally filed, and at, for example, page 10, lines 11-17.

New Claim 31 is introduced. Support for this claim can be found throughout the specification as originally filed, and at, for example, page 7, lines 26-27, and the paragraph bridging pages 8 and 9.

No new matter is added by way of this Amendment. Entry and consideration of this Amendment are respectfully requested.

Withdrawn Rejections

1. Applicants thank the Examiner for withdrawing the rejection of Claims 25-27 under 35 U.S.C. §112, first paragraph.

2. Applicants thank the Examiner for withdrawing the rejection of Claims 25-27 under 35 U.S.C. § 102(e).

3. Applicants thank the Examiner for withdrawing the rejection of Claims 1 and 3-6 under 35 U.S.C. § 103(a).

Claim Objections

1. On page 2 of the Office Action, Claim 1 is objected to because the first step (a) allegedly should recite "incubating…"

2. On page 2 of the Office Action, Claim 1 is further objected to because the "microinjecting" step is alleged to use improper grammar.

Applicants respectfully submit that the amendments to Claim 1 attached herewith fully address the issues raised in the objections.

Withdrawal of the objections is respectfully requested.

Claims 1 and 3-6 are Definite Under 35 U.S.C. § 112

On page 3 of the Office Action, Claims 1 and 3-6 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

1. In one aspect of the rejection, the Examiner contends that recitation of "the early embryo thereof" in Claim 1 lacks antecedent basis.

2. In a second aspect of the rejection, the Examiner contends that Claim 1 is indefinite because "at a stage except for and after the blastodermic stage just after egg laying... ...wherein the early embryo is at least 24 after the start of incubation" lacks a nexus.

Applicants respectfully submit that the amendments to Claim 1 fully address the issues raised in the rejection, and that the claims as amended are definite under 35 U.S.C. § 112, 2nd paragraph. For example, recitation of "the early embryo" in Claim 1 finds explicit antecedent basis, and Claim 1 as amended does not recite "at a stage except for and after the blastodermic stage just after egg laying," rendering the second aspect of the rejection moot.

Withdrawal of the rejection is respectfully requested.

Claims 1 and 3-6 are Patentable Under 35 U.S.C. § 102

1. On page 4 of the Office Action, Claims 1, 3, 5 and 6 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Harvey *et al.* (*Nat. Biotech.*, 2002, 19: 396-399).

In making the rejection, the Examiner contends that Harvey *et al.* discloses a transgenic G1 chicken obtained by microinjecting a Stage X embryo with a replication-defective retroviral vector encoding a protein, allowing the embryo to develop to term and hatch, thereby obtaining a G0 chick, and mating the G0 chick after reaching sexual maturity. The Examiner further contends that the timing of vector administration is of no consequence to the structure of the transgenic chicken, to justify the assertion that the transgenic chicken of Harvey *et al.* is structurally the same as a transgenic chicken produced by injecting an egg at 24 or 48 hours after laying.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Relevant law holds that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." (Emphasis added.) *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir 1987).

First, Applicants note that Claim 1 as amended recites that the replication-deficient retroviral vector codes "for an antibody," and that the antibody content of the avian is not lower than 5μg/ml in blood, not lower than 1μg/ml in egg white, and not lower than 1μg/ml in egg yolk. Applicants respectfully note that the vector of Harvey *et al.* encodes β-lactamase, not an antibody. Accordingly, the structure of the avians of the presently claimed invention are structurally different from those of Harvey *et al.* at least with respect to the *transgene* they contain.

For at least this reason, the birds of Harvey *et al.* are structurally distinct from those presently claimed.

Second, Applicants respectfully note that the timing of vector administration in Harvey *et al.* differs from that presently claimed, and that this difference in timing is of consequence to the structure of the resulting G0 and G1 transgenic birds, or progeny thereof.

Specifically, Applicants respectfully point out that, at the time of the invention, different nomenclature was employed by different groups to define the stages of early embryo development, as follows. One approach, discussed in Hamburger and Hamilton (*Journal of Morphology,* 1951, 88:49-92), delineated 46 chronological stages between egg-laying and hatching. In contrast, the approach discussed in Eyal-Giladi and Kochav (*Developmental*

Biology, 1976, 49: 321-337) describes, *see* Abstract, that stages I-XIV precede stage 2 of Hamburger and Hamilton. In other words, stage XIII of the nomenclature of Eylal-Giladi and Kochav corresponds to a stage prior to stage 2 in the nomenclature of Hamburger and Hamilton; Applicants note that stage 2 in the nomenclature of Hamburger and Hamilton occurs at 7 hours after the start of incubation. *See* page 54 of Hamburger and Hamilton. Further, the correspondence between these two nomenclatures was well known in the art at the time of the invention.[1]

Turning to Harvey *et al.*, the Examiner acknowledges that Harvey *et al.* discloses vector administration at Stage X; as would be recognized by those of ordinary skill in the art, *see* *Poultry Science*, 1997, 76:83-90,[2] this stage thus corresponds to a stage that is, *at the latest*, 7 hours after egg laying. Accordingly, Harvey *et al.* administer the vector by 7 hours after egg laying, whereas the G0 transgenic birds of the presently claimed invention are produced by vector administration at least 24 hours after egg laying. Accordingly, the method of Harvey *et al.* is different from that presently claimed, at least with respect to the timing of administration of the vector.

---

[1] *See, e.g.*, *Poultry Science*, 1997, 76:83-90. On page 83, right column, it is described that Eyal-Giladi and Kochav categorized early chicken development - prior to stage 2 of Hamburger and Hamilton, into 14 stages; it is also described that Eyal-Giladi and Kochav used Roman numerals to distinguish their stages from that of Hamburger and Hamilton, who used Arabic numerals.

[2] In accordance with M.P.E.P. 609(c), the document cited herein in support of Applicants' remarks is being submitted as evidence directed to an issue raised in the Official Action, and no fee pursuant to 37 C.F.R. 1.97 or 1.98, or citation on a FORM PTO/SB/08 or PTO-1449 is believed to be necessary.

In this regard, and in contrast to that asserted by the Examiner,[3] Applicants respectfully submit that this difference in timing does impart a structural difference to the transgenic avians of the presently claimed invention vis-à-vis those of Harvey *et al.*, and one such difference is recited in the claims as amended. Specifically, Claim 1 recites the degree of expression of the transgene in the blood, egg white, and egg yolk, of transgenic avians; namely that it is expressed in an amount of at least 20μg/ml in blood, at least 5μg/ml in egg white, and at least 1μg/ml in egg yolk. As already noted on the record,[4] high levels of transgene expression can be effected by administering the claimed replication-deficient retroviral vector at least 24 hours after the start of the incubation, and as shown by Tables 1-4 in the instant specification, this characteristic of high transgene expression - as a result of avoiding transgene silencing - is inherited by the G1 and G2 transgenic birds. Accordingly, in addition to the presently claimed avians differing from those of Harvey *et al.* with respect to the structure of the transgene they possess, and the structure of the expression *product* of the transgene therein, the avians of the claimed invention are structurally different from those of Harvey *et al.* also with respect to the amount of the *product* of the transgene produced - such high expression being probative of the novelty and non-obviousness of the present invention.

Withdrawal of the rejection is respectfully requested.

[3] *See* page 5, 1st paragraph, of the outstanding Office Action.

[4] *See* page 17 of the Amendment filed November 13, 2009.

2. On page 5 of the Office Action, Claims 1, 3, 5 and 6 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Rapp *et al.* (*Transgenic Res.*, 2003, 12: 569-575) as evidenced by Speksnijder *et al.* (*Poultry Sci.*, 2000, 79: 1430-1433).

In making the rejection, the Examiner contends that Rapp *et al.* discloses a transgenic chicken obtained by microinjecting a Stage X embryo with a replication-defective retroviral vector encoding a protein, allowing the embryo to develop to term and hatch, thereby obtaining a G0 chick, and mating the G0 chick after reaching sexual maturity. The Examiner further contends that the timing of vector administration is of no consequence to the structure of the transgenic chicken, to justify the assertion that the transgenic chicken of Rapp *et al.* is structurally the same as a transgenic chicken produced by injecting an egg at 24 or 48 hours after laying.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants respectfully submit that the presently claimed invention is novel and nonobvious for the same reasons as asserted above in response to the rejection over Harvey *et al.* For example, Rapp *et al.* employ a structurally different transgene, *i.e.*, interferon α-2b. Accordingly, the presently claimed avians differ from those of Rapp *et al.* with respect to the structure of the transgene they possess, and the structure of the expression *product* of the transgene.

Further, Rapp *et al.* administer the vector at Stage X, *i.e.*, by 7 hours after egg laying, whereas the G0 transgenic birds of the presently claimed invention are produced by vector administration at least 24 hours after egg laying. Thus, the method of production of Rapp *et al.* is different from that presently claimed, at least with respect to the timing of administration of

the vector. As discussed above, this difference in timing does impart a structural difference to the transgenic avians of the presently claimed invention vis-à-vis those produced by vector administration by 7 hours, such as enhanced expression of the transgene.

Withdrawal of the rejection is respectfully requested.

3. On page 7 of the Office Action, Claims 1 and 3-6 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by MacArthur *et al.* (U.S. Patent No. 6,825,396).

In making the rejection, the Examiner contends that MacArthur *et al.* discloses a transgenic avian obtained by microinjecting a Stage X embryo with a replication-defective retroviral vector encoding a protein, allowing the embryo to develop to term and hatch, thereby obtaining a G0 chick, and mating the G0 chick after reaching sexual maturity. The Examiner further contends that the timing of vector administration is of no consequence to the structure of the transgenic chicken, to justify the assertion that the transgenic chicken of MacArthur *et al.* is structurally the same as a transgenic chicken produced by injecting an egg at 24 or 48 hours after laying.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants respectfully submit that the presently claimed invention is novel and nonobvious for the same reasons as asserted above in response to the rejection over Harvey *et al.* For example, MacArthur *et al.* employ a structurally different transgene, *i.e.*, beta-galactosidase, in their working examples. Accordingly, the presently claimed birds differ from those actually produced by MacArthur *et al.* with respect to the structure of the transgene they possess, and the structure of the expression *product* of the transgene.

Further, even assuming *arguendo* MacArthur et *al.* suggests that an antibody transgene may be used, at no point does MacArthur *et al.* explicitly describe a transgenic avian containing the presently claimed levels of antibody transgene expression, *i.e.*, at least 20μg/ml in blood, at least 5μg/ml in egg white, and at least 1μg/ml in egg yolk. For reasons already discussed above, *i.e.*, that administration of the vector at Stage X, *i.e.*, by 7 hours after egg laying (which the method of MacArthur *et al.* does) results in transgene silencing - whereas the production method recited in instant Claim 1 does not - avians produced by the method of MacArthur *et al.* would not *necessarily* produce antibody at the recited levels, as would otherwise be required to sustain the rejection (under a theory of inherency).

Withdrawal of the rejection is respectfully requested.

4. On page 8 of the Office Action, Claims 1 and 3-6 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Ivarie *et al.* (U.S. Patent No. 6,730,822).

In making the rejection, the Examiner contends that Ivarie *et al.* discloses a transgenic avian obtained by microinjecting Stage VII-XII embryos with a replication-defective retroviral vector encoding a protein. The Examiner also appears to contend that the timing of vector administration is of no consequence to the structure of the transgenic avian, to justify the assertion that the transgenic avian of Ivarie *et al.* is structurally the same as a transgenic avian produced by injecting an egg at 24 or 48 hours after laying.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants respectfully submit that the presently claimed invention is novel and nonobvious for the same reasons as asserted above in response to the rejection over Harvey *et al.*

For example, Ivarie *et al.* employ a structurally different transgene, *i.e.*, beta-galactosidase, in their working examples. Accordingly, the presently claimed birds differ from those actually produced by Ivarie *et al.* with respect to the structure of the transgene they possess, and the structure of the expression *product* of the transgene.

Further, even assuming *arguendo* that Ivarie *et al.* suggests that an antibody transgene may be used, at no point does Ivarie *et al.* explicitly describe a transgenic bird containing the presently claimed levels of antibody transgene expression, *i.e.*, at least 20μg/ml in blood, at least 5μg/ml in egg white, and at least 1μg/ml in egg yolk. For reasons already discussed above, *i.e.*, that administration of the vector by 7 hours after egg laying (which the method of Ivarie *et al.* does) results in transgene silencing - whereas the production method recited in instant Claim 1 does not - birds produced by the method of Ivarie *et al.* would not *necessarily* produce antibody at the recited levels, as would otherwise be required to sustain the rejection (under a theory of inherency).

Withdrawal of the rejection is respectfully requested.

5. On page 9 of the Office Action, Claims 1 and 3-6 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Sang *et al.* (U.S. Patent Application Publication 2005/0273872), as evidenced by Kamachi *et al.* (*Development*, 1998, 125:2521-2532).

In making the rejection, the Examiner contends that Sang *et al.* discloses a transgenic avian obtained by microinjecting Stage X-XIII embryos with a replication-defective retroviral vector encoding a protein.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants respectfully submit that the presently claimed invention is novel and nonobvious for the same reasons as asserted above in response to the rejection over Harvey *et al.* For example, Sang *et al.* employ a structurally different transgene, *i.e.*, beta-galactosidase, in their working examples. Accordingly, the presently claimed birds differ from those actually produced by Sang *et al.* with respect to the structure of the transgene they possess, and the structure of the expression *product* of the transgene.

Further, even assuming *arguendo* that Sang *et al.* suggests that an antibody transgene may be used, at no point does Sang *et al.* explicitly describe a transgenic bird containing the presently claimed levels of antibody transgene expression, *i.e.*, at least 20μg/ml in blood, at least 5μg/ml in egg white, and at least 1μg/ml in egg yolk. For reasons already discussed above, *i.e.*, that administration of the vector by 7 hours after egg laying (which the method of Sang *et al.* does) results in transgene silencing - whereas the production method recited in instant Claim 1 does not - birds produced by the method of Sang *et al.* would not *necessarily* produce antibody at the recited levels, as would otherwise be required to sustain the rejection (under a theory of inherency).

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Alan C. Townsley/

Alan C. Townsley, Ph.D.
Registration No. 64,740

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: February 15, 2011